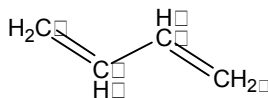


1,3-BUTADIENE
CAS No. 106-99-0

First Listed in the *Fifth Annual Report on Carcinogens* as *Reasonably Anticipated to be a Human Carcinogen* -- changed to *Known to be a Human Carcinogen* in the *Ninth Report on Carcinogens*



CARCINOGENICITY

1,3-Butadiene is *known to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in humans, including epidemiological and mechanistic information, which indicate a causal relationship between occupational exposure to 1,3-butadiene and excess mortality from lymphatic and/or hematopoietic cancers.

In 1989, 1,3-butadiene was first listed in the Fifth Annual Report on Carcinogens as “*reasonably anticipated to be a human carcinogen*” based on evidence of its carcinogenicity in experimental animals. Subsequent to the initial animal cancer findings, 1,3-butadiene has been shown to be metabolized to mutagenic and carcinogenic epoxides (epoxybutene and diepoxybutane) in all mammalian species studied, including humans. In addition, a number of human epidemiology studies have been published including (1) a cohort study showing excess risk for lymphosarcoma and reticulosarcoma in workers who manufactured 1,3-butadiene monomer, (2) a significantly increased risk for leukemia among production workers in a study of styrene-butadiene rubber workers in eight plants in the United States and Canada, and (3) a large excess of leukemia that was associated with exposure to 1,3-butadiene and not to styrene in a case-control study within the cohort of styrene-butadiene rubber workers (IARC 1992). In addition, Ward *et al.* (1996) found an excess of lymphosarcoma and reticulosarcoma among 1,3-butadiene production workers in a previously unstudied chemical plant. When compared to the standardized mortality ratio for leukemia in the U.S. population, Matanoski *et al.* (1993) reported that this ratio was 1.8 times higher in long-term workers who were hired before 1960 and who had worked in three of the eight previously studied styrene-butadiene rubber plants. A second case-control study of the lymphopoietic cancers among styrene-butadiene rubber workers (new set of controls per case) confirmed the strong association and significant dose-response effect between increasing 1,3-butadiene exposure score and increasing risk for leukemia (Matanoski *et al.* 1993). Finally, a follow-up study of styrene-butadiene rubber workers concluded that exposure to 1,3-butadiene in the synthetic rubber industry produced a dose-related increase in the occurrence of leukemia (Macaluso *et al.* 1996, Delzell *et al.* 1996).

The evidence that butadiene is a human carcinogen is supported by experimental animal studies which have shown that 1,3-butadiene induces benign and malignant neoplasms at multiple tissue sites in multiple species, and supporting mechanistic data. Experimental studies in laboratory animals demonstrated that 1,3-butadiene is carcinogenic to mice and rats at multiple organ sites. Sites of tumor induction in mice included the hematopoietic system, heart (hemangiosarcomas), lung, forestomach, harderian gland, preputial gland, liver, mammary gland, ovary, and kidney (Huff *et al.* 1985, Melnick *et al.* 1990, NTP 1984). Sites of tumor induction in rats included the pancreas, testis, thyroid gland, mammary gland, uterus, and Zymbal gland (Owen *et al.* 1987).

ADDITIONAL INFORMATION RELEVANT TO CARCINOGENESIS OR POSSIBLE MECHANISMS OF CARCINOGENESIS

Mouse, rat, and human liver microsomes have been shown to oxidize 1,3-butadiene to epoxybutene (Csadány *et al.* 1992) and further oxidize the monoepoxide to diepoxybutane (Seaton *et al.* 1995). These metabolites form *N'*-alkylguanine adducts. These adducts have been detected in liver DNA of mice exposed to 1,3-butadiene and identified in the urine of a worker exposed to 1,3-butadiene. Activated *K-ras* genes and inactivated tumor suppresser genes observed in 1,3-butadiene-induced tumors in mice are analogous to genetic alterations frequently observed in a wide variety of human cancers. Dose-related increases in *hprt* mutations have been observed in lymphocytes isolated from mice exposed to 1,3-butadiene or its epoxide metabolites and in occupationally exposed workers. The mutational spectra for 1,3-butadiene and its epoxide metabolites at the *hprt* locus in mouse lymphocytes are similar to the mutational spectrum of ethylene oxide, an alkylating agent listed as a *known to be human carcinogen* (NTP 2000). The mechanism of tumor induction by 1,3-butadiene in rodents and humans appears to be due to its metabolism to DNA-reactive intermediates resulting in genetic alterations in protooncogenes and/or tumor suppressor genes.

PROPERTIES

1,3-Butadiene is a colorless, non-corrosive gas with a mild aromatic or gasoline-like odor. When heated, 1,3-butadiene emits acrid fumes. It is both explosive and flammable, and a dangerous fire hazard when exposed to heat, flame, or powerful oxidizers. When exposed to air, it will also form explosive peroxides that are sensitive to shock or heating above 27°C, and will explode upon contact with aluminum tetrahydroborate. 1,3-Butadiene is sparingly soluble in water, more soluble in methanol and ethanol, and soluble in most common organic solvents such as acetone, diethyl ether, benzene, and cyclohexane. It readily polymerizes in the presence of sodium or oxygen, and explosive peroxides may form when it is exposed to air (Budavari 1996, HSDB 2000, Lewis 1992). The commercial product is 99% pure. It may contain part per million (ppm) levels of butadiene dimer (NTP 1993).

Because 1,3-butadiene is a highly volatile gas at room temperature, it is transported to consumers as a liquefied gas under pressure (Morrow 1990). Means of transportation include pipeline, barge, tank car, and tank truck. During transportation, 1,3-butadiene contains an antioxidant inhibitor such as tert-butylcatechol, hydroquinone, or di-n-butylamine (Kirshenbaum 1985).

USE

1,3-Butadiene is used primarily as a chemical intermediate and polymer component in the manufacture of synthetic rubbers. Seventy-five percent of 1,3-butadiene produced is used in synthetic rubber manufacture (Morrow 1990). In 1986, 95% of 1,3-butadiene produced in the United States was used for the production of styrene-butadiene rubber (SBR) (32.7%), polybutadiene rubber (22.3 %), adiponitrile (12.5%), styrene-butadiene latex (9.9%), chloroprene (6.6%), acrylonitrile-butadiene-styrene (ABS) resins (4.4%), nitrile rubber (2.7%), and other uses, including export (3.9%). The major end-use products for most of these copolymers are tires (84% of SBR and 75% of the polybutadiene in North America) and nylon products (adiponitrile) (Kirschner 1996). Butadiene is also used in the manufacture of the fungicides, captan and captafol. The polymers are used in the manufacture of latex adhesives, various rubber

products, nylon carpet backings, paper coatings, pipes, conduits, appliance and electrical equipment components, and luggage (SRI 1982, JACA Corp. 1987).

PRODUCTION

1,3-Butadiene is isolated by distillation or extraction from crude butadiene, which is a by-product of ethylene production. In 1996, 3.8 billion lb (1.7 million metric tons or Mg) of 1,3-butadiene was produced, making it the 36th largest chemical product in the United States (Chem. Eng. News 1997). According to Chemical Market Associates Inc., global 1,3-butadiene consumption is anticipated to increase by 4.1% annually. Projected global production of 1,3-butadiene for the year 2001 was 18.5 billion lb (8.4 million Mg), with North American production being 5.5 billion lb (2.5 million Mg). *Chemical and Engineering News* reported that rubber grade 1,3-butadiene production held steady in 1990 with almost 3.2 billion lb produced domestically (Chem. Eng. News 1991). This value was consistent with annual production figures for 1988 and 1989 (USITC 1989, 1990). This value was roughly a 10% increase over the 1987 total of 2.9 billion lb (USITC 1988, 1989). In 1986, approximately 2.6 million lbs of 1,3-butadiene were produced in the United States (USITC 1987). In 1985, the United States produced over 2.3 billion lb (USITC 1986). Thirteen domestic manufacturers of 1,3-butadiene produced a total of nearly 2.8 billion lb in 1984 (USITC 1985). In 1983, over 2.3 billion lbs of 1,3-butadiene were produced in the United States (USITC 1984). U.S. production in 1982 was reported to be nearly 1.9 billion lb (USITC 1983). In 1981, the United States produced almost 3.0 billion lb (USITC 1982).

1,3-Butadiene world imports were approximately 1.38 billion lb in 2000 (ITA 2001) and 338 million lb in 1989 (USDOC Imports 1990). According to ITA (2001), 37.6 million lbs were exported from the United States in 2000. In 1987, the United States imported over 823 million lb of 1,3-butadiene (USDOC Imports 1987). In 1985, the United States imported 832 million lb and exported over 187 million lb of 1,3-butadiene (USDOC Exports 1986). In 1984, 158.2 million lb of 1,3-butadiene were exported and 837 million lb were imported (USDOC Exports 1985). In 1983, 96.5 million lbs of 1,3-butadiene were exported and nearly 885 million lbs were imported (JACA Corp. 1987, Chem. Week 1984). In 1982, imports of 1,3-butadiene were 867.7 million lb, and exports were 102.5 million lb (Chem. Week 1984). In 1981, the United States imported nearly 458 million lb and exported 122 million lb of 1,3-butadiene (SRI 1982).

EXPOSURE

The primary routes of potential human exposure to 1,3-butadiene are inhalation, ingestion, and dermal contact (HSDB 2000). Manufacturing, transporting, or using 1,3-butadiene are among the major anthropogenic sources of 1,3-butadiene releases to the environment (ATSDR 1992, Eastern Research Group, USA 1996). Sources of 1,3-butadiene emissions include facilities producing 1,3-butadiene, styrene-butadiene copolymer, polybutadiene, neoprene, acrylonitrile-butadiene-styrene (ABS) copolymer, nitrile elastomer, and adiponitrile. Lesser emissions are discharged by facilities producing styrene-butadiene-vinylpyridine (SBV) latex, butadiene-vinylpyridine latex, tetrahydrophthalic anhydride, captan, captafol, 1,4-hexadiene, dodecanoic acid, butadiene dimers, methyl methacrylate-[acrylonitrile]-butadiene-styrene resins, ethylidene norbornene, butadiene-furfural cotrimer, sulfolane, and 1,3-butadiene cylinders, and poly(vinyl chloride). Because 1,3-butadiene is an impurity at 6 ppm in vinyl chloride monomer, 1,3-butadiene emissions of 210 µg per kilogram poly (vinyl chloride) (PVC) have been estimated for PVC production (Eastern Research Group, USA 1996).

Occupational exposure to 1,3-butadiene may occur through inhalation and, to a lesser extent, dermal contact (NTP 1984). The National Occupational Exposure Survey (NOES) conducted by the National Institute for Occupational Safety and Health (NIOSH) from 1981-1983 estimated that 51,971 total workers, including 1,411 women, at 2,201 facilities were potentially exposed to 1,3-butadiene (NIOSH 1990). The National Occupational Hazard Survey (NOHS), conducted by NIOSH from 1972 to 1974, estimated that 69,555 workers were potentially exposed to 1,3-butadiene in the workplace (NIOSH 1976). The NOHS indicated that 44,980 workers (69% of the total number of workers potentially exposed) were employed in the chemical and allied products industry; 9,086 workers (14%) were employed in the rubber and plastics products industry; 5,339 workers (8%) were employed in miscellaneous business services; and 2,244 workers (3.4%) were employed in various manufacturing industries (NIOSH 1984a). Health Hazard Evaluation surveys conducted by NIOSH at six facilities indicated that exposures to 1,3-butadiene in those facilities were significantly below the 1984 OSHA permissible exposure limit (PEL) of 1,000 ppm as an 8-hr time-weighted average (TWA). The range of reported exposures was 0.06 to 39 ppm. The types of facilities surveyed included those which manufactured helmets and visors, synthetic rubber, rubber tires and tubes, automotive weather stripping, braided hoses, and plastic components for aircraft (NIOSH 1984b).

Osterman-Golkar *et al.* (1996) monitored (using stationary and personal monitoring) 17 workers in the 1,3-butadiene production unit in a Swedish petrochemical plant to determine workplace exposure. Average exposure for workers handling 1,3-butadiene containers was $11.2 \pm 18.6 \text{ mg/m}^3$ ($5.06 \pm 8.41 \text{ ppm}$). Maintenance and laboratory workers exposure was 1.2 mg/m^3 (0.54 ppm). These concentrations were determined by analyses of personal and area full shift air sample.

NIOSH conducted studies to determine 1,3-butadiene exposure in monomer, polymer, and end-user industries. Workers in five job areas were classified as having potentially higher exposure to 1,3-butadiene. These five areas included maintenance technician (0.026 to 94.38 mg/m^3 ; 0.012 to 42.7 ppm), loading (0.17 to 273 mg/m^3 ; 0.08 to 123 ppm), tank farm (0.02 to 52.8 mg/m^3 ; 0.009 to 24 ppm), process (i.e., purification, polymerization, and reaction) (<0.011 to 76.78 mg/m^3 ; <0.0050 to 34.7 ppm), and laboratory (<0.0132 to 822.8 mg/m^3 ; <0.006 to 372 ppm). Exposure concentrations were determined from personal or area full-shift air samples. Exposure of workers in the monomer industry, based on personal full-shift and short-term air samples (including subcategories of laboratory technician and process technician), ranged from <0.02 to 374 ppm (<0.04 to 827 mg/m^3). Personal exposure of workers in the polymer industry (including laboratory technician, tank farm operator, front end [reaction], maintenance technician, and back end [finishing]) ranged from <0.005 to 42.9 ppm (<0.01 to 94.9 mg/m^3) for full-shift samples and 0.087 to 280 ppm for short-term exposures. Full-shift (0.19 to 619 mg/m^3) area air samples in the polymer industry indicated 1,3-butadiene exposure ranging from less than 0.006 to 9.01 ppm (<0.01 to 19.9 mg/m^3). For the monomer industry as a whole, 1,3-butadiene concentrations were $>10 \text{ ppm}$ (22 mg/m^3) in 7.1% of the samples, 2 to 10 ppm (4 to 22 mg/m^3) in 12.8%, 1 to 2 ppm (2 to 4 mg/m^3) in 12.3% and $<1 \text{ ppm}$ in 67.8% (the present OSHA permissible limit is 1 ppm). For the polymer industry as a whole, the corresponding percentages for these 4 ranges were 3.3%, 7.7%, 3.3%, and 85.8%, respectively. The arithmetic mean exposure for personal full-shift exposures in the polymer plants was 1.14 ppm (2.57 mg/m^3) (Fajen *et al.* 1993).

Of 184 facilities reporting on 1,3-butadiene emissions to the U.S. EPA for the 1995 Toxic Chemical Release Inventory (TRI), 175 reported a total of 2,913,561 lb of 1,3-butadiene released to air. Total nonpoint air emissions were 1,437,468 lb from the 169 facilities reporting nonpoint air emissions such as process venting and equipment leaks (TRI95 1997). TRI95 (1997) reported releases of 1,3-butadiene to surface water totaling 5,398 lb, while a total of 277 lb of 1,3-

butadiene was released to land in 1995. EPA's TRI listed 145 industrial facilities that produced, processed, or otherwise used 1,3-butadiene in 1988 (TRI88 1990). The facilities reported releases of 1,3-butadiene to the environment which were estimated to total 68 million lb. In 1999, total on-site reported release of 1,3-butadiene was 1,914,443 pounds (TRI99 2001).

A nationwide 1,3-butadiene inventory (including vehicle emissions and emissions from manufacturing and producing facilities) calculated annual butadiene emissions to air to be 102,000 Mg/yr for the year 1990 (Ligocki *et al.* 1994), considerably higher than the TRI88 (1990) reports of 2,294 Mg/yr for industrial emissions. Calculations were based on butadiene emission factors for the various emission sources considered.

1,3-Butadiene is emitted from furnaces at secondary lead smelting facilities handling automotive lead-acid batteries that contain plastic battery separators or that have hard rubber casings. In 1992, petroleum refineries were the fourth largest emitters of 1,3-butadiene with 1,3-butadiene being released from blowdown vents, catalyst regeneration process vents, and miscellaneous vents at vacuum distillation, alkylation, and thermal cracking units (Eastern Research Group, USA 1996).

Volatilization of 1,3-butadiene from wastewaters of styrene-1,3-butadiene copolymer production at publicly owned treatment works (POTW) has been calculated to be 21 tons/yr (19 Mg/yr) (Eastern Research Group, USA 1996).

1,3-Butadiene is naturally formed as a byproduct of forest fires (HSDB 2000). Emissions from wood burning in a wood-stove and small-scale model experiments showed that 1 to 2% by weight of total non-methane hydrocarbons emitted were 1,3-butadiene (Barrefors and Peterson 1995).

Incomplete combustion of a variety of fuels forms 1,3-butadiene as a product. 1,3-Butadiene comprises 0.5 to 2% of the total organic gas emissions from most types of combustion (Ligocki *et al.* 1994). It can also be found in exhaust emissions from motor vehicles as a product of incomplete combustion of gasoline and diesel oil and from the thermal breakdown of plastics (ATSDR 1992, Eastern Research Group, USA 1996).

California has run dispersion modeling from a typical freeway source and has estimated that gasoline-fueled vehicles emit 0.011 g/mi (Cooper and Reisman 1992). Ligocki *et al.* (1995a) calculated that on road gasoline vehicle exhaust contained 0.59% 1,3-butadiene by weight. Diesel vehicle exhaust contained 1.55% 1,3-butadiene by weight.

Cigarette smoke is also an environmental source of 1,3-butadiene. Releases into the air in sidestream smoke have been variously estimated at 152 to 400 µg 1,3-butadiene per cigarette (Ligocki *et al.* 1995b). Calculations based on 400 µg/cigarette indicate that 1,3-butadiene concentrations in the homes of smokers would be increased by approximately 4 µg/m³, and concentrations in air at workplaces allowing smoking would increase by 13 µg/m³ (Wallace 1991).

Certain cooking oils release 1,3-butadiene when heated. For example, 1,3-butadiene emissions were approximately 22-fold higher from heated unrefined Chinese rape seed oil than from heated peanut oil. Of three fatty acids tested, heated linolenic acid produced the greatest amount of 1,3-butadiene. Although cooking oils in the United States are refined for purity, U.S. rape seed oil (canola) also emitted 1,3-butadiene (Shields *et al.* 1995).

The Chemical Manufacturers Association (CMA) studied baseline volatile organic

chemical (VOC) measurements in Washington, D.C., from March 12, 1990 to March 11, 1991. 1,3-Butadiene was detected in 26.79% of the samples collected for 24-hour periods, once every 6 days. Preliminary results indicated a mean 1,3-butadiene concentration of 0.13 ± 0.17 ppb (0.29 ± 0.38 $\mu\text{g}/\text{m}^3$). The maximum concentration observed was 0.83 ppb (1.8 $\mu\text{g}/\text{m}^3$). The mean was calculated using randomly generated values between zero and the detection limit for all samples in which butadiene was below the limit of detection. Washington, D.C. was selected since it was one of the largest cities that did not contain large industrial air pollution sources (Hendler and Crow 1992).

Outdoor 1,3-butadiene concentrations in six United States urban settings were in the range of 0.3 to 1.6 $\mu\text{g}/\text{m}^3$ (0.14 to 0.72 ppb) (Wallace 1991). California's statewide population-weighted exposure to ambient (outdoor) airborne 1,3-butadiene was estimated to be an average of 0.37 ppb (0.82 $\mu\text{g}/\text{m}^3$). One-hour outdoor concentrations ranged to a high of 17.7 ppb (39.1 $\mu\text{g}/\text{m}^3$). Similar indoor concentrations were observed in taverns where heavy smoking conditions existed (Seiber 1996).

Additional exposure information is presented in other available documents (ATSDR 1992, Eastern Research Group, USA 1996).

REGULATIONS

EPA regulates 1,3-butadiene under the Clean Air Act (CAA), the Toxic Substances Control Act (TSCA), the Resource Conservation and Recovery Act (RCRA), and the Superfund Amendment and Reauthorization Act (SARA). 1,3-Butadiene is listed as a hazardous air pollutant, and emission standards have been established under the CAA. It is subject to the submission of information relating to the release of toxic chemicals under Section 313 of Title III of SARA (1986), and health and safety data reporting under TSCA. The Superfund (CERCLA, SARA) reportable quantity (RQ) for 1,3-butadiene is 10 lb. Notification of EPA is required if the RQ level or greater is released to the environment.

FDA regulates 1,3-butadiene as an indirect food additive.

NIOSH recommends that the exposure limit of the compound be the lowest feasible concentration. OSHA has set the permissible exposure limit (PEL) of 1 ppm (2.2 mg/m^3) as an 8-hr time-weighted average (TWA) for 1,3-butadiene, with a 15-minute short-term exposure limit (STEL) of 5 ppm. OSHA also regulates 1,3-butadiene under the Hazard Communication Standard and as a hazardous chemical in laboratories. Regulations are summarized in Volume II, Table 25.

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